

REMARKS

After amending the claims as set forth above, claims 53, 56, 63-65, 67, 68, 76 and 85-92 will be pending in this application.

Claim 53 has been amended to clarify the invention for better understanding by the Examiner. No new matter has been added by this change. Furthermore, Applicant submits that the amendment does not limit the claim scope and that the terms "derived" and "obtained" have similar meaning and scope in the context of the claim. New claims 85 to 92 find basis in the application as filed including, for example, at page 11, lines 1-12, page 15, lines 28-33, and page 16, lines 11-18. Accordingly, the new claims raise no issue of new matter.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 53, 63-68 and 76 have been rejected under 35 U.S.C. § 112, first paragraph for lacking written description for the phrase "at least a portion of the variable region of an immunoglobulin light chain." The Examiner alleges that this phrase introduces new matter that goes beyond the specification which is alleged to cover only specific antibody fragments previously known in the art. The rejection is respectfully traversed.

Relevant Law

To satisfy the written description requirement of 35 U.S.C. § 112, ¶1, the specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, the applicant was in possession of the claimed invention. *See, e.g., Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991). Compliance with the written description requirement is essentially a fact-based inquiry that will necessarily vary depending on the nature of the invention claimed. *See, e.g., Enzo Biochem. Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1324, 63 U.S.P.Q.2d 1609, 1612 (Fed. Cir. 2002).

Response to statements by the Examiner

The Examiner argues that Applicant's cited support in the specification is not sufficient because the "language at pages 11, 15, and 16 refer to immunoglobulin light chain portions in the context of the composition of specific antibody fragments, namely an Fv fragment and an abzyme." Paper No. 23, page 4. Applicant notes from this statement that the Examiner agrees that the cited portions of the patent specification provide written description support for cells with nucleic acid encoding "at least a portion of the variable region of an immunoglobulin light chain." However, the Examiner appears to maintain the rejection because the cited text allegedly does not also support the limitation for the cells to not contain nucleic acid encoding a heavy chain.

Applicants wishes to point out that the preparation of cells that produce only one chain of a two chain immunoglobulin is well described in the application. For example, the specification at page 14, line 30 to page 15, line 7 describes an approach for inserting nucleic acid encoding a first and second polypeptides into separate cells to form first and second transformants. These transformants are later combined to yield hybrid progeny. This concept of first and second transformants is further detailed in the specification at page 16, line 22 to page 22, line 31. Thus, when the teachings of the specification as a whole are taken into account, one of ordinary skill in the art would understand that the specification describes cells with nucleic acid encoding at least a portion of the variable region of an immunoglobulin light chain while the cells do not contain nucleic acid encoding a heavy chain. Both limitations are therefore inherent in the discussion of dual chain immunoglobulin and fragments described at pages 11, 15 and 16 of the specification.

Furthermore, Applicant respectfully disagrees with the Examiner's statement that the claim language in question encompasses polypeptides with as "few as one amino acid." Paper No. 23, page 4. The only rationale offered to support this position is that "the limitation refers to the variable region of the light chain from which the portion was obtained." *Id.* Applicant cannot discern a supporting rationale from this statement and requests that the Examiner provide a more clear explanation for the basis of the rejection or withdraw the rejection. Any such explanation would need to account for the claimed

requirement that the at least a portion of the variable region of an immunoglobulin light chain be capable of forming an antigen-specific immunoglobulin when co-expressed in a plant cell with said heavy chain from said antigen-specific immunoglobulin. In this regard, it is noted that if the light chain portion were to read on a single amino acid, as the Examiner alleges, such single amino acid could not form an antigen specific immunoglobulin with the heavy chain as required.

In view of the above, it is respectfully submitted that the specification provides adequate written support for the claim language. Accordingly, reconsideration and withdrawal of the rejection is earnestly solicited.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The rejection of Claim 53 under 35 U.S.C. § 112, second paragraph as being indefinite because of the word "derived" is respectfully traversed. The Examiner alleges that "derived" does not indicate how much of the light chain is "derived" from by the antigen specific immunoglobulin. It is respectfully submitted that this constitutes circular reasoning and does not state any basis to support why derived is indefinite. Nevertheless, Applicant has amended the claim to recite that the immunoglobulin light chain is "obtained" from an antigen specific immunoglobulin. It is Applicant's position that both terms mean the same in this context.

Furthermore, Applicant maintains that "derived" is not indefinite because the skilled artisan would understand that this term properly reflects that various lengths of light chain are encompassed under the claim by virtue of the limitation "at least a portion of the variable region of an immunoglobulin light chain. When one skilled in the art would understand all of the language in the claims when read in light of the specification, a claim is not indefinite. *Rosemount Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 1547, 221 USPQ 1, 7 (Fed. Cir. 1984), *Caterpillar Tractor Co. v. Berco, S.P.A.*, 714 F.2d 1110, 1116, 219 USPQ 185, 188 (Fed. Cir. 1983). Accordingly, the rejection is without basis and should be withdrawn.

REJECTION UNDER 35 U.S.C. § 102 OVER GOODMAN

The rejection of claims 53, 56, 63, 64, 67, 68 and 76 under 35 U.S.C. § 102(b) as allegedly being anticipated by Goodman (U.S. Patent no. 4,956,282) is respectfully traversed.

Relevant Law

In order to anticipate a claim, a single prior art reference must provide each and every element set forth in the claim. *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). See also, MPEP §2131. The Examiner bears the initial burden of establishing a *prima facie* case of anticipation. Only when a *prima facie* case has been established does the burden shift to the applicant to rebut the *prima facie* case. See, e.g., *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997).

Response to statements by the Examiner

The Examiner maintains that Goodman teaches a plant cell that contains a nucleic acid encoding at least a portion of the light chain variable region but not a heavy chain. The only support for this proposition is a single sentence in Goodman, at column 3, lines 20-22, quoted below.

Structural genes of interest include α -, β - and γ - interferons, immunoglobulins, with the structural genes coding for the light and heavy chains and desirably assembly occurring in the plant cell

Notably deficient from the rejection is any indication of how this meager statement teaches to express the light chain or a portion thereof in plants without a heavy chain. As already indicated in related cases, Applicant points out that the word "desirably" would be understood to refer to assembly of the two chains in cells as opposed to assembly *in vitro*. It is respectfully submitted that Goodman fails to disclose an essential element of the claims, that plant cells contain nucleotide sequence encoding an immunoglobulin

product comprising at least a portion of the variable region of an immunoglobulin light chain but not nucleotide sequence encoding and immunoglobulin heavy chain. **If the Examiner should maintain the rejection, Applicant respectfully requests that the Examiner identify the precise language in Goodman that supports this teaching.**

It is further noted that the Examiner's argument that "a plant cell that expresses an individual heterologous polypeptide would have been within the abilities of one skilled in the art at the time of filing" is wholly irrelevant to the determination of whether a reference anticipates a claim. Paper no. 23, page 7. As already mentioned, anticipation requires the Examiner to identify where each and every element of the claim is found in a single reference. The fact that one skilled in the art has the ability to use an invention says nothing about whether the art teaches the invention. The same reasoning undercuts the Examiner's other stated rationale for the rejection, that "Goodman's expression of a heterologous interferon polypeptide in plant cells would reasonably have been considered to advance the possibility of expressing any single chain heterologous polypeptide in a plant cell." *Id.*

As the rejection for anticipation fails to identify in Goodman an essential element of claims 53, 56, 63, 64, 67, 68 and 76 (and the newly added claims), the Examiner is earnestly solicited to withdraw the rejection.

REJECTION UNDER 35 U.S.C. § 103 OVER GOODMAN

The rejection of claim 65 under 35 U.S.C. § 103(a) as being allegedly obvious over Goodman and Applicant's admitted prior art is respectfully traversed.

Relevant Law

To establish a *prima facie* case of obviousness, three criteria must be met; there must be some motivation or suggestion, either in the cited publications or in knowledge available to one skilled in the art, to modify or combine the cited publications; there must be a reasonable expectation of success in combining the publications to achieve the

claimed invention; and the publications must teach or suggest all of the claim limitations. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP § 2142. In analyzing obviousness, the Court of Appeals for the Federal Circuit has repeatedly cautioned that:

[t]he factual inquiry... must be based upon objective evidence of record....
[T]he best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references....
[P]articular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed.

In re Sang-Su Lee, 277 F.3d 1338, 1343 (Fed. Cir. 2002) (internal citations omitted).

Response to statement raised by the Examiner

The Examiner appears to support the rejection of claim 65 on the following arguments (see Paper No. 23, page 8-9):

- 1) That Goodman teaches a plant cell that contains a nucleic acid encoding at least a portion of the light chain variable region but not a heavy chain;
- 2) That gamma interferon, although structurally and functionally distinct immunoglobulin, are both heterologous to plants;
- 3) While gamma interferon is a single polypeptide and the immunoglobulin light chain is the natural member of a heterodimer, expression of immunoglobulin light chain in heterologous systems was known; and
- 4) the claim limitation that the light chain be capable of forming an antigen specific immunoglobulin when co-expressed with a heavy chain is an inherent feature of the light chain.

Applicant's rebuttal to each argument is separately provided below.

1) Goodman fails to teach a plant cell that contains a nucleic acid encoding at least a portion of the light chain variable region but not a heavy chain

The deficiencies of the Goodman reference were discussed in detail under the rejection for anticipation. As amply demonstrated therein, Goodman fails teach expression of an immunoglobulin light chain without a heavy chain.

2) That gamma interferon, although structurally and functionally distinct from immunoglobulin, are both heterologous to plants

Applicant does not dispute that both gamma interferon and immunoglobulin are both heterologous to plants. However, it is respectfully submitted that being foreign to a plant undercuts rather than supports the rejection. The Examiner is respectfully requested to clarify how this bare fact supports the rejection and is distinguished from point number 3.

3) While gamma interferon is a single polypeptide and the immunoglobulin light chain is the natural member of a heterodimer, expression of immunoglobulin light chain in heterologous systems was known

The Examiner appears to be arguing that alleged success in expressing light chain alone in heterologous systems other than plants would have caused the ordinary skilled artisan to believe that there would have been a reasonable expectation of success to translate this to expression in plants. The facts, however, weigh against this view.

A critical fact ignored by the Examiner which demonstrates the non-obviousness of the claimed invention (and the deficiencies of the instant rejection) is During's failed attempt to express an immunoglobulin light chain in plants from a vector that did not encode a heavy chain. This was described in the During dissertation, page 80 line 2 where During stated that "[r]epeated attempts to directly detect the light chain of B1-8 and for T4 lysozyme from crude extracts of tobacco-mesophyll protoplasts were unsuccessful." See During dissertation and Lerner declaration filed March 8, 2002. This

failure of During is a clear teaching away that would negate any obvious rejection based on the Goodman patent and/or any other reference of record.

In addition, as acknowledged by the Examiner, gamma interferon is structurally and functionally distinct from an immunoglobulin light or heavy chain. Interferon is naturally a single polypeptide while an immunoglobulin light chain is a member of an immunoglobulin heterodimer. The Lerner Declaration supports as much when it stated that "the ability to express each individual chain (light or heavy) was unexpected . . ." Lerner Declaration, ¶ 25.

The file history of the Goodman patent reinforces Applicant's view that the differences between interferon and immunoglobulin were considered significant. The Goodman patent issued from U.S. application serial no. 760,236 filed July 29, 1985. First, none of Goodman's original claims were directed to expressing immunoglobulin or for that matter any heterodimer in plants. Original claims of 760,236 are attached as EXHIBIT 1. Thus, the originally filed claims indicate that Goodman never seriously considered that his discovery could be extended to immunoglobulin. Furthermore, the Patent Office rejected Goodman's claims for lack of enablement because they extended to single polypeptides other than interferon, the only exemplified embodiment.

Claims 1-5, 7, 8, 10 and 11 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to Agrobacterium-mediated dicot transformation with chimeric genes comprising opine synthase promoters and structural genes encoding human interferon or antibiotic resistance as per pages 10-18. . . . Given the unpredictability inherent in the art, undue experimentation would be required by one of ordinary skill in the art to determine DNA sequences for non-disclosed mammalian peptides or promoters and to develop transformation vectors resulting in detectable expression of stable, bioactive peptides as claimed in claims 1-5, 8, 10 and 11.

U.S. serial No. 760,236, Office Action 6/9/87, pages 3-4 (Office Action attached as EXHIBIT 2). Goodman failed repeatedly to convince the examiner to withdraw the lack of enablement rejection and eventually appealed the case to the Board of Patent Appeals and Interferences. On September 29, 1989, the Board affirmed the rejection for non-

enablement. The Board's decision makes clear as quoted below that the patent is not enabling for any mammalian peptide other than interferon.

It appears to have been accepted by the examiner that the experimental portion of appellants' specification enables one of ordinary skill in the relevant art to repeat that which appellants have done, i.e., obtain the expression of an interferon gene through the use of a transformed Ti-plasmid in dicotyledonous plant cells. In view of the very same high order unpredictability of success in extrapolating reported procedures to different systems, e.g., different genes, different vectors, and different hosts, discussed above, appellants' arguments that their disclosure enables one of ordinary skill to practice the inventions claimed more generally in the broader claims without the exercise of undue experimentation are unreasonable on their face.

BPAI Decision, page 4-5 (BPAI decision attached as EXHIBIT 3). The position of the Board supports Applicants' view that Goodman does not enable expression in plants of any immunoglobulin.

4) The claim limitation that the light chain be capable of forming an antigen specific immunoglobulin when co-expressed with a heavy chain is an inherent feature of the light chain.

It is respectfully submitted a case for non-obviousness of claim 65 has be made without resort to the limitation that the encoded immunoglobulin product comprising at least a portion of the variable region of an immunoglobulin light chain be capable of forming an antigen specific immunoglobulin when co-expressed with the heavy chain is not needed to support patentability. Nevertheless, Applicant wishes to point out that the Examiner's assertion of inherency is unsupported and in conflict with the fact that During attempted and failed to express a light chain without a heavy chain.

Accordingly, for all the above reasons, it is respectfully submitted that rejection of claim 65 as allegedly being obvious over Goodman is without basis and should be withdrawn.

CONCLUSION

Applicant believes that the present application is now in condition for allowance.
Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is urged to contact the undersigned by telephone to address any outstanding issues standing in the way of an allowance.

Respectfully submitted,

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